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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application

Applicant(s): Rigoutsos et al.  
Docket No.: YOR920000435US1  
Serial No.: 09/712,638  
Filing Date: November 14, 2000  
Group: 1631  
Examiner: Cheyne D. Ly

I hereby certify that this paper is being deposited on this date with the U.S. Postal Service as first class mail addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Signature:  Date: October 22, 2004

Title: Unsupervised Building and Exploitation of Composite Descriptors

TRANSMITTAL OF SUPPLEMENTAL APPEAL BRIEF

Mail Stop Appeal Brief - Patents  
Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

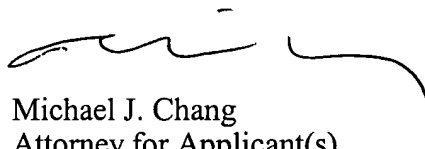
Sir:

Submitted herewith are the following documents relating to the above-identified patent application:

1. Supplemental Appeal Brief (original and two copies); and
2. Request to Reinstate Appeals.

There is an additional fee of \$340 due in conjunction with this submission under 37 CFR §1.17(c). Please charge **IBM Corporation's Deposit Account No. 50-0510** the amount of \$340 to cover this fee. In the event of non-payment or improper payment of a required fee, the Commissioner is authorized to charge or to credit **IBM Corporation's Deposit Account No. 50-0510** as required to correct the error. Duplicate copies of this letter and two copies of the Appeal Brief are enclosed.

Respectfully,



Date: October 22, 2004

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Attorney Docket: YOR920000435US1

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REQUEST TO REINSTATE APPEAL

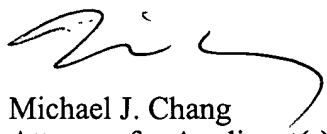
Mail Stop Appeal Brief – Patents  
Commissioner for Patents  
P.O. Box 1450  
Arlington, VA 22313-1450

Sir:

Applicants hereby request reinstatement of the appeal. Applicants' Appeal Brief was submitted on April 27, 2004 and a Corrected Appeal Brief was submitted on July 19, 2004. A New Office Action was mailed on September 29, 2004.

The attention of the Examiner and the Appeal Board to this matter is appreciated.

Respectfully,



Date: October 22, 2004

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Examiner: C.D. Ly

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Signature: *Vin. Maurio* Date: October 22, 2004

Title: Unsupervised Building and Exploitation of Composite Descriptors

SUPPLEMENTAL APPEAL BRIEF

Mail Stop Appeal Brief – Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Appellants hereby reply to the non-final Office Action, mailed September 29, 2004. A request to reinstate the appeal is submitted herewith. Appellants' Appeal Brief in an appeal of the final rejection of claims 1-12, 23 and 25 in the above-identified patent application was submitted on April 27, 2004 and a Corrected Appeal Brief was submitted on July 19, 2004 (referred to herein collectively as "Appellants' Appeal Briefs").

REAL PARTY IN INTEREST

A statement identifying the real party in interest is contained in Appellants' Appeal Brief.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences that will directly affect or be directly affected by or have a bearing on the decision in the present appeal.

STATUS OF CLAIMS

Claims 1-12, 23 and 25 are pending in the above-identified patent application. A statement identifying the original status of the claims is contained in Appellants' Appeal Briefs. Claims 4 and 7 are now rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Further, claims 1-12, 23 and 25 are now rejected under 35 U.S.C. §101, as allegedly being directed to non-statutory algorithm type subject matter. Claims 1-8, 10-12, 23 and 25 are now rejected under 35 U.S.C. §102(b) as allegedly unpatentable over the article entitled "GenBank" by Benson et al. (hereinafter "Benson") and claims 1-12 are now rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Benson taken with the article by Kleffe et al., entitled "GeneGenerator-A Flexible Algorithm For Gene Prediction And Its Application To Maize Sequences," BIOINFORMATICS, vol. 14, no. 3, pgs. 232-243 (1998) (hereinafter "Kleffe").

STATUS OF AMENDMENTS

A statement identifying the status of the amendments is contained in Appellant's Appeal Briefs.

SUMMARY OF INVENTION

A Summary of the Invention is contained in Appellant's Appeal Briefs.

ISSUES PRESENTED FOR REVIEW

A statement identifying the issues originally presented for review is contained in Appellant's Appeal Briefs. In the present Office Action, the Examiner has withdrawn the previous rejections and has added new rejections. Accordingly, the following new issues are presented for review.

- i. Whether claims 4 and 7 are properly rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention;
- ii. Whether claims 1-12, 23 and 25 are properly rejected under 35 U.S.C. §101 as being allegedly directed to non-statutory algorithm type subject matter;
- iii. Whether claims 1-8, 10-12, 23 and 25 are properly rejected under 35 U.S.C. §102(b) as being allegedly unpatentable over Benson; and

iv. Whether claims 1-12 are properly rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Benson taken with Kleffe.

### GROUPING OF CLAIMS

For the purpose of addressing the new grounds of rejection, claims 1-3, 10, 12, 23 and 25 stand or fall together. Claim 4 stands or falls alone. Claims 5 stands or falls alone. Claim 6 stands or falls alone. Claim 7 stands or falls alone. Claim 8 stands or falls alone. Claim 9 stands or falls alone. Claim 11 stands or falls alone.

### CLAIMS APPEALED

A copy of the appealed claims is contained in Appendices of Appellant's Appeal Briefs.

### ARGUMENT

#### Rejections under 35 U.S.C. §112, second paragraph

Claims 4 and 7 are rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. In the Office Action, page 3, 2<sup>nd</sup> paragraph, the Examiner stated that,

[s]pecific to the limitation of 'without using any knowledge about properties or features of sequences', said limitation causes claim 4, which depends from claim 1, to be vague and indefinite because claim 1 recites 'the sequences are not aligned.' The recitation of 'the sequences are not aligned' in claim 1 has been reasonably construed as providing 'knowledge about properties or features of sequences.' Therefore, the step of discovering without 'knowledge about properties or features of sequences' in claim 4 is unclear since 'knowledge about properties or features of sequences' has been previously provided in claim 1.

Appellants respectfully submit that the step of "discovering . . . without using any knowledge about properties or features of sequences in the set of unaligned sequences" is defined in the specification in such a way that the metes and bounds of claim 4 are clearly ascertainable. Namely, the Examiner's assertion that the sequences not being aligned is "knowledge about properties or features" of the sequences is wholly in contravention to the teachings of the claims and supporting specification.

First, the instant specification sets forth, at page 8, lines 6-7, that prior to the instant techniques, "researchers knew and exploited properties of the sequences, knew and exploited features of

the sequences, and/or aligned the sequences.” By way of example only, the specification on page 7, lines 19-23, sets forth the definition of a feature, e.g., in a computational biology context, as,

a combination of amino acids with understood behavior and possibly known 3-dimensional structure. For instance, for a helix-turn-helix (HTH) motif that mediates the binding of many regulatory proteins to regulatory control sites of DNA, the two features are the two helices at the beginning (7 a.a.) and the end (9 a.a.) of the 20 a.a. stretch that corresponds to an instance of the HTH motif.

Further, the specification, at page 7, lines 23-25, defines a property as,

an attribute of a feature: in the case of the HTH, a property would be the fact that the two features (helices) are held together through non-polar interactions of their side chains.

Nothing in the specification indicates that a property or a feature of a sequence that is known or used, e.g., in discovering patterns, includes the fact that the sequences are not aligned, as the Examiner suggests. In fact, claim 4, itself, recites that “discovering is performed without using any knowledge about properties or features of sequences in the set of unaligned sequences.” (emphasis added) Respectfully, one of ordinary skill in the art, given the teachings of claim 4 and the supporting teachings of the specification, would not interpret “without using any knowledge about properties or features of sequences” to include using the fact that the sequences are not aligned, because, if one were to follow this unsubstantiated interpretation, claim 4 would be inconsistent, and make no sense.

Further, in regard to claim 4, the Examiner in the Office Action, page 3, 3<sup>rd</sup> paragraph, stated that,

The limitation of ‘unaligned sequences’ causes claim 4 to be vague and indefinite because claim 1, line 2, from which claim 1 [sic.] depends, recites ‘not aligned.’ Claim 4 is unclear whether the limitations are the same. Further the antecedent basis for said limitations are unclear because of the inconsistency of said limitations.

The Examiner seems to be questioning whether the terms “unaligned” and “not aligned” are the same. Appellants respectfully submit that one of ordinary skill in the art, given the teachings of the claims and supporting specification, would recognize that the terms “unaligned” and “not aligned” are used synonymously, and as such, would be able to ascertain the metes and bounds of claim 4. For example, claim 1 recites, in part, “providing a set of sequences, wherein the sequences are not aligned.” (emphasis added) Support for this limitation in the specification, e.g., at page 6, line 13, recites taking a set of “unaligned” sequences.

Further, by way of example only, Merriam-Webster’s Collegiate Dictionary, tenth edition, defines the term “unaligned” simply as “nonaligned,” e.g., the equivalent of “not aligned.”

As mentioned above, claim 7 is also rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Namely, the Examiner stated in the Office Action, at page 3, 4<sup>th</sup> paragraph, that,

[regarding claim 7] the limitation of ‘for one of the positions . . . one expected symbol is a plurality of expected symbols’ causes said claim to be vague and indefinite because it is unclear whether ‘one of the positions’ is occupied by one symbol or a plurality of symbols.

Appellants respectfully submit that the metes and bounds of claim 7 are ascertainable from the teachings of the claims and supporting specification. For example, Claim 6, from which claim 7 depends, recites, in part, that “each pattern comprises a plurality of positions, some of the plurality of positions each comprise at least one expected symbol.” (emphasis added) Claim 7 recites, in part, that “the at least one expected symbol is a plurality of expected symbols.” It is important to keep in mind that this limitation of claim 7 refers to the pattern(s). The specification, at page 13, lines 1-3, for example, indicates that a bracket, e.g., in a pattern, represents a “one of” choice. For instance, the exemplary pattern shown in the specification, at page 25, line 21, illustrates some positions being occupied by “one of” a plurality of symbols. As such, the limitations of claim 7 are not indefinite.

As such, Appellants respectfully request reconsideration and withdrawal of the Section 112 rejection.

#### Rejections under 35 U.S.C. §101

Claims 1-12, 23 and 25 are rejected under 35 U.S.C. §101, as allegedly being directed to non-statutory algorithm type subject matter. Namely, the Examiner in the Office Action, page 4, 4<sup>th</sup> paragraph, stated that,

[c]laims 1-12, 23, and 25 are rejected because said claims are directed to a method, system, and an article of manufacture comprising steps for analyzing sequence data without any physical alteration step, which is considered to be non-statutory subject matter. . . [T]he instant invention comprises algorithmic steps for analyzing sequence data without any physical alteration resulted from said analysis.

The Examiner in the Office Action, page 4, 5<sup>th</sup> paragraph, further stated that,

[i]t is acknowledged that claims 23 and 25 are directed to a system and an article of manufacture comprising computer components for processing sequence data. However, the processing steps achieved by said computer components do not

cause any physical alteration outside of the system or article of manufacture resulted from said processes.

Appellants respectfully disagree with the Examiner's assertions. Under Section 101,  
 5 "any new and useful process, machine, manufacture, or composition of matter" is patentable. 35 U.S.C. §101. It is recognized, however, that despite the broad scope of section 101, "laws of nature, physical phenomena and abstract ideas" cannot be patented. *Diamond v. Chakrabarty*, 447 U.S. 303, 309, 206 U.S.P.Q. (BNA) 193, 197 (1980). The Examiner asserted that claims 1-12, 23 and 25 appear to claim  
 10 "algorithmic steps for analyzing sequence data." To the contrary, however, each of independent claims 1, 23 and 25 are expressly directed to a practical application. Namely, in each of claims 1, 23 and 25 it is determined whether a candidate sequence comprises a predetermined number of patterns common to a plurality of unaligned sequences, i.e., to determine whether the candidate sequence is a member of a family. See, for example, page 6, lines 14-15, of the specification. Thus, "the present invention provides a way of determining in an unsupervised manner additional members for a family that is  
 15 defined initially through exemplar sequences." Specification, page 6, lines 1-3.

Therefore, each of claims 1, 23 and 25, as well as all claims dependent thereon, are clearly tied to a practical application. A process that is limited to a practical application of an abstract idea or mathematical algorithm in the technological arts is patentable. See Examination Guidelines for Computer-Related Inventions, Section IV. B. 2. b. (ii). For at least this reason, Appellants submit that  
 20 each of claims 1-12, 23 and 25 are in full compliance with 35 U.S.C. §101, and accordingly, respectfully request that the rejections under 35 U.S.C. §101 be withdrawn.

#### Rejections under 35 U.S.C. §102

Claims 1-8, 10-12, 23 and 25 are rejected under 35 U.S.C. §102(b) as allegedly  
 25 unpatentable over Benson. To the extent that the arguments presented in Appellants' Appeal Brief are pertinent to the present rejections and cited art, those arguments are maintained and incorporated by reference herein. The additional remarks and rejections made by the Examiner in the present Office Action will now be addressed.

In the Office Action, page 5, 5<sup>th</sup> paragraph, the Examiner stated that,  
 30 UniGene [(a subset of GenBank)] comprises clusters of EST sequences wherein said EST sequences are not complete and have not been characterized (unaligned), as in instant claim 4. ESTs are screened against each other to determine those likely to be derived from the same gene and sequences share [sic.] statistically significant DNA similarity (common patterns) are placed into the same



cluster, as in instant claim 5. One important use of the UniGene clusters (set of sequences) is to identify novel and non-redundant sequence candidates that identifies coding sequences in the genome based on predetermined patterns of said clusters, as in instant claims 1-3. (internal citations omitted)

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The Examiner makes reference to an NCBI News article, dated August 1996 (hereinafter "NCBI News") to support the rejections.

Regarding claims 1-3, Appellants respectfully submit that clustering sequences, as described in Benson, does not anticipate, nor make obvious, the step of discovering patterns common to a plurality of sequences, e.g., as in claim 1, from which claims 2 and 3 depend. Namely, nowhere does Benson teach or suggest discovering any patterns. Clustering similar sequences simply is not the same as pattern discovery, even if the clustering is based on "significant DNA similarity." For at least that reason, the teachings of the present claims are neither anticipated nor obvious over Benson.

Claim 4, as described above, recites that the step of discovering is performed without using any knowledge about properties or features of sequences in the set of unaligned sequences. As would be apparent to one of ordinary skill in the art, the fact that the sequences described in Benson are not characterized, as alleged by the Examiner, does not, in any way indicate that they are not aligned. As such, Benson contains no teaching directed to the alignment, or lack thereof, of the sequences. Further, as described above in conjunction with the rejection of claim 1, Benson does not teach or suggest pattern discovery. Therefore, for that reason alone, claim 4 is neither anticipated nor obvious over Benson.

Claim 5 recites, in part, that if the candidate sequence comprises the predetermined number of patterns, then that sequence is added to the set of sequences to create a new set of sequences. First, as described above in conjunction with the rejection of claim 1, Benson does not teach or suggest pattern discovery. Therefore, for that reason alone, claim 5 is neither anticipated nor obvious over Benson. Further, Benson does not teach or suggest setting a "predetermined number" criteria. By way of example only, NCBI News, in a more detailed explanation of the teachings contained in Benson, merely states that sequences sharing statistically significant DNA sequence similarity in the 3' UTR are assigned to the same cluster. See, NCBI News, page 3. Therefore, no predetermined number criteria, as in the present claims, is employed.

Regarding instant claims 8 and 11, in the Office Action, page 6, 1<sup>st</sup> paragraph, the Examiner stated that,

[t]he UniGene set serves as a source of mapping candidates and as a standard to compare and screen new EST submissions. ESTs are screened against

each other to determine those likely to be derived from the same gene and sequences share statistically significant (predetermined threshold) DNA similarity (common patterns), and placed into the same cluster. New EST submissions that do not match any sequences (predetermined threshold) in the UniGene set are considered (selected) new human genes and are organized into unique clusters to provide additional mapping candidates, as in instant claims 8 and 11. (internal citations omitted)

Claim 8 recites that the step, e.g., of claim 3, of determining if each of the plurality of patterns is statistically significant comprises the steps of selecting one of the patterns, determining if a probability that the selected pattern occurs in a sequence meets a predetermined threshold, and continuing to select additional patterns until each pattern has been selected.

For at least the reason, as presented above in conjunction with the rejection of claim 1, that Benson does not teach or suggest pattern discovery, claim 8 is neither anticipated nor obvious over Benson.

Claim 11 recites that the step, e.g., of claim 3, of determining if each of the plurality of patterns is statistically significant further comprises the steps of if any of the patterns is statistically significant, selecting a statistically significant pattern, modifying a composite descriptor to include the selected pattern if the selected pattern is not already part of the composite descriptor, and continuing to select statistically significant patterns until all statistically significant patterns have been selected.

As above, e.g., regarding the rejection of claim 1, for at least the reason that Benson does not teach or suggest pattern discovery, claim 11 is neither anticipated nor obvious over Benson. Further, as presented above, NCBI News, in a more detailed explanation of the teachings contained in Benson, merely states that sequences sharing statistically significant DNA sequence similarity in the 3' UTR are assigned to the same cluster. See NCBI News, *Id.* Nothing, therefore, in Benson and/or NCBI News in any way indicates collecting statistically significant information, patterns or otherwise, e.g., in a composite descriptor.

With regard to claims 6 and 7, the Examiner, in the Office Action, beginning on page 6, 4<sup>th</sup> paragraph, stated that,

[i]n BLAST, statistical significance scores are calculated a set of probabilities for the occurrence of individual residues (at least one expected symbol), and for aligning pairs of residues (plurality of positions). BLAST measures well-defined mutation scores (occupied by any sequence character) and detects biologically significant sequence similarities, as in instant claim 6 and 7. (internal citations omitted).

In making the above statement, the Examiner cited pages 406-408 of the article by Altschul et al., entitled, "Basic Local Alignment Search Tool," 215 J. MOL. BIOL. 403-410 (1990) (hereinafter "Altschul").

Claim 6 recites, in part, that each pattern, e.g., of claim 1, comprises a plurality of positions, some of the plurality of positions each comprise at least one expected symbol and other of the plurality of positions comprise positions which may be occupied by any sequence character.

As was described in Appellants' previous Appeal Briefs, BLAST does not involve pattern discovery. For example, BLAST, as referenced in Benson and described in Altschul, does not have anything to do with the processing of sequences in a set of sequences. Namely, BLAST does not generate anything, pattern or otherwise, from the sequences in a set of sequences. BLAST is in fact a query-driven method that involves processing a query sequence to aid in finding matches with that query in a database of sequences. Specifically, BLAST takes a query sequence and processes it to generate sequential  $k$ -tuples, wherein the value of  $k$  is fixed. For example, see Altschul, page 405, first col., wherein a list of all contiguous  $w$ -mers in the query sequence is generated, e.g., often with  $w = 12$ . The  $k$ -tuples generated are then compared to sequences in a database. See Altschul, *Id.* Therefore, BLAST does not anticipate discovering patterns common to a plurality of sequences in a set of sequences and then determining if a candidate sequence comprises a number of the patterns. For at least this reason, the teachings of the present claims are neither anticipated nor obvious over Benson.

Secondly, BLAST would not be a suitable program to determine whether certain patterns exist in a candidate sequence. As mentioned above, BLAST functions by generating tuples, e.g.,  $w$ -mers, from a query sequence. Trying to match one or more patterns with a sequence, by processing the sequence (as in BLAST) would make finding any matches nearly impossible. Therefore, the teachings of Benson are inconsistent with the present teachings. For at least this reason, the teachings of the present claims are neither anticipated nor obvious over Benson. Thus, for at least that reason, claim 6 is neither anticipated by, nor obvious over, Benson. Further, BLAST does not involve a search criteria having one of either positions that each comprise at least one expected symbol and positions which may be occupied by any sequence character.

Claim 7 recites, that for one of the positions, e.g., of claim 6, the at least one expected symbol is a plurality of expected symbols. For at least the reason that BLAST does not involve pattern discovery, as described above in conjunction with the rejection of claim 6, claim 7 is neither anticipated by, or obvious over, Benson. Further, as was highlighted above, e.g., in reference to claim 6, BLAST

does not involve a search criteria having positions that each comprise at least one expected symbol, e.g., a plurality of expected symbols.

As such, Appellants respectfully request reconsideration and withdrawal of the rejection of claims 1-8, 10-12, 23 and 25 under 35 U.S.C. §102(b).

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Rejections under 35 U.S.C. §103

Claims 1-12 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Benson taken with Kleffe. Namely, the Examiner in the Office Action, beginning on page 8, 4<sup>th</sup> paragraph, stated that,

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Benson et al. does not disclose the limitation of using a second-order Markov chain method. . . . Kleffe et al. discloses an improvement for using second-order Markov chain method to predict gene structure. . . . An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Kleffe et al. and utilize the second-order Markov chain method in the method of Benson et al. for discovering new genes. Therefore it would have been obvious to one having ordinary skill in the art at the time of the invention was made [sic.] to use the gene discovery method of Benson et al. and Kleffe et al. with the second-order Markov chain method.

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First, Appellants respectfully submit that, as presented above, the teachings of the present claims are neither anticipated nor obvious over Benson. Kleffe does not provide any of the limitations for which Benson is lacking. Thus, for at least that reason, claims 1-12 are not obvious over Benson taken with Kleffe.

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The Examiner further stated in the Office Action, page 8, 5<sup>th</sup> paragraph, that in Kleffe “[t]he second-order Markov chain method is used to determined [sic.] the natural logarithm of the probability of a specific sequence (pattern) occur [sic.] in the *Arabidopsis* sequences, as in instant claim 9.” (internal citations omitted) A review of the teachings of Kleffe, however, reveal no teaching or suggestion of the concept of patterns, but merely the derivation of Markov models using probability functions. As such, Appellants respectfully submit that there is no teaching in Kleffe directed to patterns.

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Therefore, Appellants respectfully request reconsideration and withdrawal of the rejection of claims 1-12 under 35 U.S.C. §103(a).

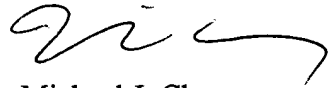
Conclusion

The rejections of the claims under §112, §101, §102 and §103 are believed to be improper and should be withdrawn.

The attention of the Examiner and the Appeal Board to this matter is appreciated.

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Respectfully submitted,



10 Date: October 22, 2004

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